The Future of TB Laboratory Services

A Framework for INTEGRATION / COLLABORATION / LEADERSHIP

Task Force Members

Kathleen G. Beavis MD
Cook County Hospital

John Bernardo MD
Massachusetts TB Control Program

Eric Blank DrPH
Missouri State Public Health Laboratory

Ed Desmond PhD
California State Public Health Laboratory

Richard Harris PhD
Wyoming State Public Health Laboratory

Rosemary Humes MS, MT(ASCP)SM
Association of Public Health Laboratories

Michael Iademarco MD, MPH
CDC, National Center for HIV/STD/TB Prevention
Division of TB Elimination

John Ridderhof DrPH
CDC, Public Health Program Practice Office
Division of Laboratory Systems

Thomas Shinnick PhD
CDC, National Center for Infectious Diseases
Division of AIDS/STD/TB/Laboratory Research

Nancy Warren PhD
Laboratory Corporation of America
(Currently Pennsylvania Public Health Laboratory)

A Report from an APHL Task Force

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Dr. Olarae Giger, Lankenau Hospital, PA

Dr. Max Salfinger, Wadsworth Center, NY State Department of Health

Dr. Steve Hinrichs, Nebraska Public Health Laboratory

Dr. Thomas Walsh, Montgomery County TB Control, MD

Ms. Tanya Oemig, Wisconsin TB Control Program

Dr. David Warshauer, Wisconsin State Laboratory of Hygiene

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Ms. Yvonne Hale, Florida Bureau of Laboratories

Mr. Dennis Nolan, Florida Bureau of Laboratories

Dr. John Dyke, Michigan Department of Community Health

Dr. James Rudrik, Michigan Department of Community Health

Dr. Max Salfinger, New York State Wadsworth Center

Ms. Bonna Cunningham, North Dakota Department of Health

Dr. Jon Counts, University of Washington

Dr. Romesh Gautom and staff , Washington Public Health Laboratory

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EXECUTIVE SUMMARY

The diagnostic laboratory plays an essential role in the treatment, prevention, and control of tuberculosis (TB). When funding for TB laboratory services fell in the 1980s, delays in the laboratory confirmation of TB and reporting of drug-susceptibility results led to delays in initiation of therapy, prolonged infectiousness, inappropriate therapy, and missed opportunities to prevent transmission. Such delays contributed to the resurgence of TB and the emergence of multidrug-resistant TB (MDR-TB) in the early 1990s in the United States.

As part of CDC's response to the threat of MDR-TB (National Action Plan to Combat MDR-TB[3]), funding was provided to improve laboratory services and an increased emphasis was placed on providing reliable results in a timely manner. During the past decade, public health laboratories made tremendous strides in improving test performance. These improvements contributed to the resumption of the decline of the incidence of TB in the United States and the decrease in MDR-TB cases.

However, federal funding for TB laboratories has not increased since 1994, representing a substantial decline in inflation-adjusted dollars. At the same time, budget shortfalls have led many state and local governments to decrease funding for TB laboratories.

The critical next step will be to develop an integrated system that ensures timely laboratory testing and the timely flow of information among laboratorians, clinicians, and TB controllers.

Today, despite an overall decline in TB cases, TB continues to incur significant social, public health, and economic costs in the United States. About 15,000 new cases of TB disease were diagnosed in 2002 in the United States, and an estimated 10-15 million persons have latent TB infection with the attendant risk of future disease. Costly TB outbreaks still occur, and MDR-TB continues to spread. Altogether, TB-related costs approach $1 billion each year in the U.S.

To reach the goal of the elimination of TB in the United States, improvements in laboratory testing must be maintained and translated into improvements in the treatment, prevention, and control of TB. **Despite advances in laboratory methods, lack of coordination for referral of specimens and cultures continues to lead to unnecessary delays in laboratory testing, reporting, and initiation of treatment.**

The critical next step will be to develop an integrated system that ensures timely laboratory testing and the timely flow of information among laboratorians, clinicians, and TB controllers. Challenges to developing such a system include:

- Limited interaction among public health laboratories, clinical laboratories and TB controllers, all of whom may be involved in testing and/or surveillance activities prompted by a particular TB case.
- Lengthy turn-around times for laboratory confirmation of positive TB tests, possibly leading to delayed treatment, inappropriate treatment, and/or missed opportunities to prevent transmission.
- Lack of standardized recommendations or algorithms to optimize the use of new technologies in settings with varying TB incidence.
- Maintaining staff proficiency in complex test procedures in light of workforce shortages and loss of laboratory expertise as increasing numbers of experienced staff reach retirement age.
- The need to upgrade antiquated laboratory information systems.

Task Force on the Future of TB Laboratory Services

The Institute of Medicine's May 2000 report, *Ending Neglect, The Elimination of Tuberculosis in the United States,* highlights the dangers of complacency in the face of declining TB case rates and shifting public health priorities. Driven by this report and cognizant of the challenges to the TB laboratory infrastructure, in 2002 the Association of Public Health Laboratories (APHL) and the Centers for Disease Control and Prevention (CDC) commissioned a Task Force on the Future of TB Laboratory Services to develop recommendations to assure continued availability of high-quality, cost-effective TB laboratory services. The group includes representatives from APHL, CDC, clinical laboratories and the National TB Controllers Association (NTCA).

The Task Force began its work by drafting a set of principles to guide the development of recommendations for TB control partners:

- TB elimination is a public health imperative.
- Effective TB control depends on an integrated system that includes clinicians, laboratories and TB controllers.
- TB control depends on effective public-private partnerships.

- Effective TB control requires a network of public and private laboratories performing testing for diseases of public health importance.
- Public health laboratories must take a leadership role to develop the laboratory network and facilitate communication among laboratories, clinicians and TB controllers.
- Effective TB Control requires timely, complete and accurate communication among the laboratory system, TB control programs and health care providers.
- Each jurisdiction must assure access to appropriate levels of quality TB testing and complete, timely reporting.

Recommendations

Based on these principles, the Task Force formulated three key **benchmarks** for all public and private laboratories performing TB testing:

- Comprehensive assessment of available TB laboratory services to fill gaps in knowledge about the capabilities and capacities of jurisdictional laboratory networks.
- Assessment of the true costs of TB laboratory services considering all payment sources (federal, state, and private) to justify a base level of funding to support these services.
- Development of jurisdictional strategic plans to implement and maintain a systems approach to TB control.

The Task Force recommends that local success achieving these benchmarks be assessed through the use of several **outcome measures**: TB incidence rate, time to treatment initiation, average testing turn-around times, extent of adherence to CDC guidelines for AFB (acid fast bacillus) smear, culture and drug susceptibility testing, the existence of written procedures for interaction with TB control partners, and measurement of training outcomes.

In addition, the Task Force recommends the use of **jurisdictional models**—as opposed to regionalization—as an organizational paradigm for TB testing services. By allowing each state laboratory system to determine how to maximize its resources to provide rapid, reliable test results, jurisdictional models circumvent many of the problems associated with regionalization of services over a multi-state area.

Finally, the Task Force encourages ongoing economic, operational, and technical research to optimize TB laboratory services.

Dissemination

In February, 2004, the Advisory Council for the Elination of TB (ACET) voted to formally endorse and support the APHL report. The Task Force calls upon ACET and all other TB control partners—American Clinical Laboratory Association, American Society for Clinical Pathology, American Society for Microbiology, APHL, CDC, College of American Pathologists, NTCA, and others—to support the widespread dissemination and implementation of these recommendations. Such support must necessarily include adequate federal and state funding.

Laboratorians, clinicians, public health officials, administrators, and funders must work together to ensure that health care providers and TB controllers have the information they need to treat TB patients, block transmission of TB, and ultimately eliminate TB in the United States.

INTRODUCTION

Driven by the Institute of Medicine's May 2000 report, *Ending Neglect, The Elimination of Tuberculosis in the United States*[6], and by the growing need for high-quality, cost-effective tuberculosis (TB) laboratory services in a time of declining case rates and shifting public health priorities, the Association of Public Health Laboratories (APHL) and the Centers for Disease Control and Prevention (CDC) commissioned a *Task Force on the Future of TB Laboratory Services* to focus attention on this lingering, and indeed neglected, public health problem. The group includes representatives from APHL, CDC, clinical laboratories and the National TB Controllers Association (NTCA).

The primary goal of the Task Force has been to *improve TB control by promoting optimal use of laboratory services and effective information tracking and reporting.* It has worked to achieve this goal by:

- Defining issues critical to laboratorians performing TB testing, public health officials, TB controllers and health care providers.
- Creating three benchmarks to promote the use of state-of-the-art methods to deliver timely, high-quality TB laboratory services to providers and health departments.

The first benchmark—***assessment of available TB laboratory services***—is recommended as a mechanism to identify current gaps in knowledge about the capabilities and capacities of public and private TB laboratories at the state and local levels. Jurisdictions are encouraged to assess TB services on a regular basis and to make changes based on disease incidence, program needs, and the availability of new technologies to improve TB detection and identification.

The second benchmark challenges TB controllers and laboratorians to work together to ***assess the true costs of TB laboratory services*** in order to justify the funding to support these services.

Finally, recognizing the great variation in the need for laboratory services among the nation's diverse state and local TB jurisdictions, the third benchmark requires jurisdictions to address their needs by developing ***jurisdictional strategic plans*** to assure:

- Quality testing and rapid, reliable results.
- Appropriate use of new technologies.
- Development of repositories for TB isolates and ready access to fingerprinting capability.
- A timely flow of information to providers, public health officials, and laboratories.
- Availability of educational and training opportunities for clinicians, public health officials, and laboratorians addressing clinical manifestations of tuberculosis, basic disease theory, and appropriate uses of TB laboratory testing.

The Task Force hopes that collaborative efforts to comply with these benchmarks will improve education and communication among laboratorians and TB controllers, as well as other stakeholders whose participation is vital to eradicate tuberculosis in the United States: clinicians, public health officials, administrators, and funding agencies.

BACKGROUND

Starting in the mid 1980's through the early 1990's, the United States experienced an increasing incidence of TB cases and laboratorians documented the emergence of multi-drug resistant tuberculosis (MDR-TB). These trends prompted an acceleration of TB control efforts and focused greater attention on the role of the laboratory—both public and private—to support those efforts (including patient care, as well as population-based disease surveillance).

Alarmed by the threat of MDR-TB, the CDC allocated supplemental funding to strengthen state-based TB control programs and public health laboratories[3]. In particular, the agency supported public health laboratory efforts to reduce lengthy delays in testing for *Mycobacterium tuberculosis,* to improve communication between laboratorians and health care providers, and to maintain a trained workforce. Thanks to this renewed commitment to TB control, the upswing in TB cases was reversed in many, but not all, areas of the country. Unacceptably high rates persist in some large population centers and areas with substantial minority immigrant populations.

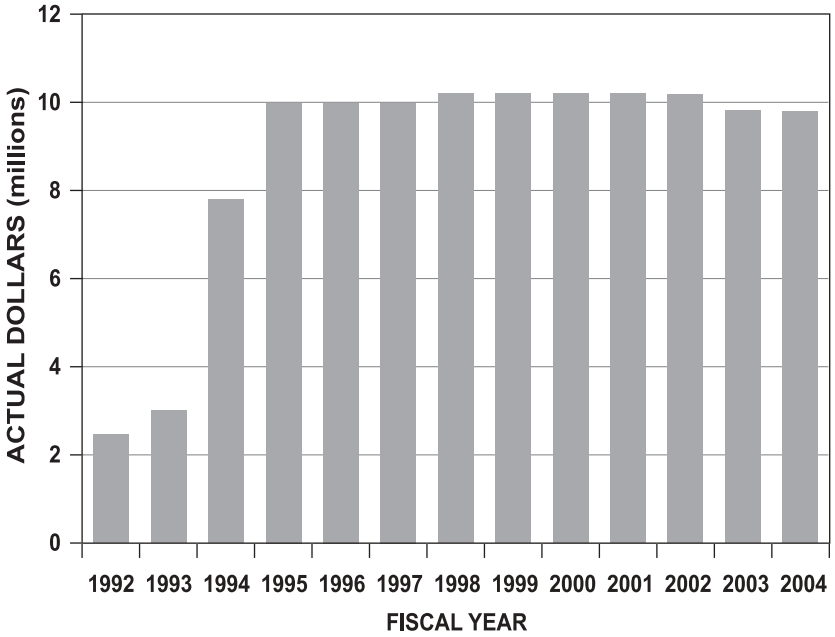

Figure 1. NCID TB Laboratory Upgrade Funding

Today, despite an overall decline in TB cases[5], TB continues to incur significant social, public health, and economic costs in the United States. About 15,000 new cases of TB disease were diagnosed in 2002 in the United States, and an estimated 10-15 million persons have latent TB infection with the attendant risk of future disease. Costly TB outbreaks still occur, and MDR-TB continues to spread. Altogether, TB-related costs approach $1 billion each year in the U.S.

Currently all 50 state public health laboratories perform some level of TB testing and serve as referral and reference laboratories for culture identification and *M. tuberculosis* drug susceptibility testing in support of other public and private sector laboratories. State public health laboratories have used CDC funding over a period of many years to create modern mycobacteriology laboratories with the latest diagnostic equipment approved for mycobacteria isolation and identification, biosafety equipment to protect laboratory staff and premises, personnel sufficient to meet the need for rapid laboratory confirmation of tuberculosis, and ongoing staff training in the use of state-of-the-art diagnostic equipment and rapid testing procedures. As laboratories have become better equipped and personnel better trained, federal funds have been used less to *upgrade* TB laboratories and more to *maintain* core TB capabilities and infrastructure.

public health mycobacteriology laboratories have fallen victim to their own success as declining funding levels once again threaten TB laboratory services in many states

In recent years, however, public health mycobacteriology laboratories have fallen victim to their own success as declining funding levels once again threaten TB laboratory services in many states. Following the initial federal funding increases, the funding level for this program has remained stagnant at about $10 million per year since 1995. Once inflation is factored in, continued level funding actually represents about a 25 percent decrease in real dollars. Compounding the fiscal situation, many state and local governments have also decreased funding for TB laboratories due to the recent economic slowdown and subsequent state belt-tightening.

Although it is tempting to think that funding can decrease in proportion to the decrease in the number of TB cases, below a certain point this reasoning falls apart, since a base level of funding (in real dollars) is necessary to maintain the TB control infrastructure. Moreover, since TB laboratory services are provided by both public and private laboratories and supported through a combination of private sector dollars, Medicare and Medicaid payments, and local, state and federal funds, it is difficult to even estimate the true cost of providing these services.

Evolving Challenges

The current uncertain funding outlook jeopardizes efforts to maintain core TB laboratory capabilities and to address the evolving challenges that hamper effective TB surveillance and response.

Communications

Researchers estimate that 80 percent of TB laboratory testing (e.g. smears and culture isolation) is performed in the private sector[12]. In fact, many large medical centers and commercial laboratories have significant capacity and capability to perform advanced TB testing. With so many entities providing varying levels of TB laboratory services and with ongoing health care system changes, including hospital mergers and the consolidation and centralization of laboratory services, the referral of specimens and isolates among laboratories is increasingly common, creating potential delays in surveillance activities and in disease treatment.

For example, a small hospital laboratory may refer a positive culture to a large commercial laboratory in another state for identification. If identified as M. tuberculosis, the commercial laboratory might perform susceptibility testing or be asked to send the culture to the public health laboratory in the state where the specimen originated for susceptibility testing and genotyping. All of these transfers prolong the testing process. Ultimately, of course, test results must be reported back to the clinician treating the patient and to the TB control program in the state where the patient resides, but the reporting route is likely to be convoluted since the specimen was handled by multiple laboratories. In the meantime, patient care may be delayed.

The limited interaction among public health laboratories, clinical laboratories and TB controllers continues to pose major challenges, emphasizing the need for an integrated and well-coordinated system for recognition, diagnosis, testing and monitoring that includes all key stakeholders: clinicians, TB controllers, and public health and private sector laboratorians. In addition, a reimbursement model based on the standard of practice for the laboratory diagnosis of TB—in which a specimen or culture from a smear-positive patient found at a local site is referred to a full service laboratory for culture and/or identification and susceptibility testing—is sorely needed.

Turn-Around Time (TAT)

Rapid detection, identification and testing for drug resistance is necessary to effectively control TB in individual patients and in populations. The Department of Health and Human Services directive *Healthy People 2010* sets a two-day target from receipt

of specimen for a laboratory to confirm and report 75 percent of culture-confirmed TB cases—a 90 percent improvement over the typical TAT in 1996[13]. Laboratory performance standards issued by the College of American Pathologists require laboratories to report TB smear results within 24 hours of specimen collection and to use liquid culture media for rapid mycobacteria detection. And current CDC testing guidelines[4], supported by APHL[9,11], recommend that:

- Laboratories receive specimens for TB testing within one day of specimen collection.
- Smear results be reported to a patient's provider within one day of specimen receipt.
- Culture identification of *M. tuberculosis* complex be reported within 21 days from specimen receipt.
- Drug susceptibility test results be reported within 30 days of specimen receipt.
- Results be reported to the local health department within one working day from the time they are reported to the specimen submitter.

Although CDC recommendations have been in effect since the mid-1990's, many laboratories are not able to meet these standards. A recent California study found that lengthy specimen transport times and the practice of conducting periodic, as opposed to daily, TB testing, are major factors that delay TB reporting. Researchers discovered that delays varied by test type and the type of laboratory performing testing and that laboratory TB test reporting often failed to conform to national guidelines and California regulations. Of concern, there was a correlation between reporting delays and treatment initiation[8].

Technological Issues

Technological advances, including the development of nucleic acid amplification tests (NAAT) and other rapid detection methods, can contribute significantly to TB control. However, there are no standardized recommendations or algorithms to optimize the use of new technologies in settings with varying TB incidence. Economic and operational research are necessary before evidence-based recommendations can be devised for laboratory services that provide for effective patient management and population-based TB control.

Workforce Competence

As the incidence of TB declines and fewer specimens are tested in many laboratories, it is difficult to maintain staff proficiency in complex TB testing procedures. Moreover,

the nation is experiencing laboratory workforce shortages ranging from 8 to more than 20 percent in different parts of the country, and expertise is being lost as increasing numbers of experienced staff reach retirement age. Many training programs for clinical laboratory scientists have closed. In the face of worker shortages, vacant positions are sometimes filled with individuals who lack training in complex laboratory science. All of these factors highlight the need for creative solutions to train staff performing TB testing and to monitor staff proficiency over time.

Laboratory Information Systems

The operation of a modern laboratory requires the integration of an information system into virtually all laboratory activities, including managing inventory, tracking specimens, reporting test results, and conveying information to epidemiologists, policy makers, and other public health partners in times of crisis. State-of-the-art information technology promises to improve the quality and organization of laboratory data and to speed the flow of information among those who need to know, thereby enhancing disease reporting and epidemiological analysis of disease trends. But the nation has yet to fully capitalize on this promise[2].

The anthrax attacks in the fall of 2001 underscore the need for integrated infectious disease surveillance systems to organize information from multiple sources, and for multiple communicable diseases (including TB), into one data repository. The National Electronic Disease Surveillance System (NEDSS), a CDC initiative, is a significant effort to achieve this result[1]. Although federal bioterrorism funds are helping to improve communications between public health and clinical laboratories, resources to develop and install modern, electronic information systems are still lacking.

Issues with Regionalization

The Institute of Medicine, in its landmark TB report, suggests regionalization as one way to increase the efficiency of public health TB testing in light of many of the challenges discussed above. This model—which would consolidate testing resources and expertise in a few locations—offers some advantages, but would also create new difficulties.

One problem inherent in regionalization is conflicting priorities that arise when funding is provided to one state or local jurisdiction to provide services for other states/jurisdictions—especially when funding is inadequate to support all TB testing needs. This problem was apparent in a CDC initiative to establish five regional centers for molecular fingerprinting of TB isolates. In some regional centers, large

test volumes led to lengthy turn-around times that rendered test results ineffective as an epidemiologic tool. Several states opted to implement spoligotyping in their own laboratories as an alternate to the restriction fragment length polymorphism (RFLP) fingerprinting method offered by the regional laboratories, even though spoligotyping provides less specific differentiation of strains than RFLP and spoligotyping results cannot be compared to RFLP results, thereby complicating the process of tracking outbreaks caused by the same TB subtype.

Other difficulties with this general model were identified in the PulseNet system for molecular fingerprinting of foodborne bacterial pathogens, which was originally instituted as a regional system. Laboratorians quickly realized that transportation and testing delays were slowing the identification of foodborne outbreaks. In addition, the system lacked sufficient capacity to support the large volume of testing necessary in outbreak situations. Needless to say, the regional paradigm was abandoned. Today, every state and several city and county public health laboratories participate in PulseNet, facilitating more rapid detection of foodborne outbreaks for a wider range of pathogens, including *Listeria monocytogenes*.

The Task Force on the Future of TB Laboratory Services finds jurisdictional models more appropriate as an organizational paradigm for TB testing services

In the early stages of planning the Laboratory Response Network (LRN), a regionalized approach was proposed for molecular detection of potential agents of bioterrorism. Early on, however, laboratorians and public health officials recognized that any system to test for agents of terrorism must offer rapid access to testing even if air transportation were not available, and that adequate national surge capacity would be essential to address public health and national security concerns. In practice, the LRN limits use of the regional model to highly specialized confirmatory testing and detection assays for BSL-4 level pathogens, which are conducted in a few laboratories with appropriate facilities and expertise.

These experiences demonstrate that regionalization is too simplistic as a generic solution to meet the TB testing needs of diverse populations across the country. The original concept of regionalization—with services consolidated in a few states—is gradually being replaced with newer models emphasizing coordination and collaboration among laboratories within state jurisdictions. The Task Force on the Future of TB Laboratory Services finds these jurisdictional models more appropriate as an organizational paradigm for TB testing services, as they allow each state laboratory system to determine how to maximize its resources to provide rapid, reliable test results.

PROCESS

APHL convened the Task Force in October 2002. Members, who are listed at the end of this report, represent:

- The Wyoming public health laboratory, which serves a state with low population and low TB incidence.
- The Missouri public health laboratory, which serves a medium size state with both urban and rural populations.
- The California state public health laboratory system, which serves a large population, including many foreign-born residents, and performs significant TB testing.
- The CDC National Center for HIV/STD/TB Prevention, Division of TB Elimination.
- The CDC Public Health Program Practice Office, Division of Laboratory Systems.
- The CDC National Center for Infectious Diseases, Division of AIDS/STD/TB Laboratory Research.
- Hospital and commercial clinical laboratories.
- The Massachusetts TB control program.

The Task Force initially agreed on a set of principles regarding the elimination of tuberculosis. These principles (listed under "Recommendations" below) guided the development of *benchmarks*—specific action items and base performance measures considered essential to improve laboratory TB services. [The Task Force adopted the concept of benchmarks from the 2002 and 2003 Supplemental Guidance to States for Bioterrorism funding. For example, in the Bioterrorism guidance document, Focus Area C, Benchmark 10 requires states to "prepare a timeline for ensuring effective working relationships and communication between Level A (Sentinel) laboratories and high level laboratories (Reference/Levels B and C.)"] Ideally, successful implementation of the benchmarks should be assessed using specific outcome measures.

An overview of Task Force activities was presented at the National Conference on Laboratory Aspects of Tuberculosis, held December 2002 in San Francisco. Conferees, including laboratory administrators, bench laboratorians, clinicians and TB controllers, expressed strong support for the Task Force and its mission, as evidenced by discussion questions and conference evaluations.

In February 2003, Task Force Chair Eric Blank provided a summary of Task Force activities, along with preliminary benchmarks, to the Advisory Council for the Elimination of TB (ACET). During a subsequent Task Force meeting that same month, the group drew from presentations of existing models for network collaboration to further develop and refine recommended benchmarks and outcome indicators.

Preliminary Task Force recommendations were presented to the APHL and NTCA memberships at their respective annual meetings in June 2003.

In February, 2004, ACET voted to formally endorse and support the APHL report, and further recommended that CDC consider the APHL recommendations when revising its laboratory guidelines.

Final recommendations will be presented to other key stakeholders, such as the American Society for Microbiology (ASM) and the American Thoracic Society (ATS), to garner their support as well.

RECOMMENDATIONS

Overall Goal

The primary goal of the Task Force is to improve TB Control through the optimal use of laboratory services and effective reporting and tracking of information.

Guiding Principles

A set of principles was drafted to guide the development of the recommendations.

- TB elimination is a public health imperative.
- Effective TB control depends on an integrated system that includes clinicians, laboratories and TB controllers.
- TB control depends on effective public-private partnerships.
- Effective TB control requires a network of public and private laboratories performing testing for diseases of public health importance.
- Public health laboratories must take a leadership role to develop the laboratory network and facilitate communication among laboratories, clinicians and TB controllers.
- Effective TB Control requires timely, complete and accurate communication among the laboratory system, TB control programs and health care providers.
- Each jurisdiction must assure access to appropriate levels of quality TB testing and complete, timely reporting.

New Paradigm for Laboratory Role

Based on these principles, the Task Force proposes a paradigm that shifts the position of the laboratory from its traditional, peripheral role in the management of TB cases and suspected cases to a central, coordinating role, in which it requests, receives and processes specimens for diagnostic and monitoring purposes and communicates information to providers and the public health agency in a timely manner to assure appropriate patient management.

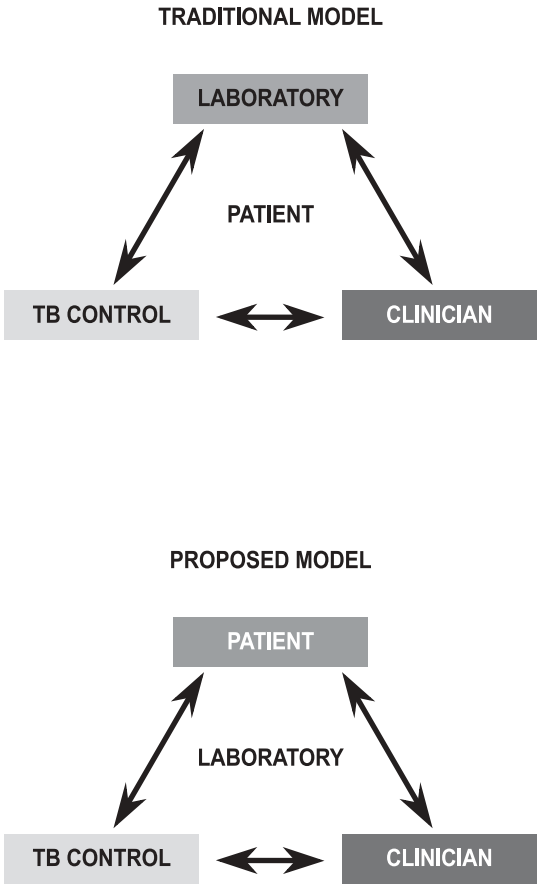

FIGURE 2.

Recommended Benchmarks to Improve Laboratory TB Services and TB Control

The Task Force recommends these specific action items and base performance measures to improve laboratory services and TB Control. Uniform implementation of these benchmarks will require new, more effective partnerships among TB controllers and public health and clinical laboratories.

Benchmark 1: Capacity and Capability

All states/jurisdictions will perform ongoing assessment of the available TB laboratory services to determine the current status and capacity of services and to identify unmet needs, obstacles to obtaining laboratory services, and opportunities for improvement. (While data are intended primarily for local use, they may also contribute to a better understanding of laboratory capacity and capability for TB testing nationally.) CDC should provide resources and technical support to develop a standardized assessment tool to assure that data are collected in a consistent manner.

Assessments should document:

- The laboratories providing TB testing services and levels (types) of services provided.
- The systems and processes for specimen referral and transport.
- Current laboratory turn-around times (TATs) for smear, culture and drug susceptibility testing.
- Barriers to meeting TAT recommendations—if current TATs fall below national standards.
- The specific laboratories that isolate *M. tuberculosis* and the availability of the isolates to the state TB control program for archiving and genotyping.
- The effectiveness of existing testing algorithms and the use of rapid technologies to meet clinician and TB control needs.
- The proficiency of all laboratorians performing TB testing.
- The ability of laboratories to rapidly detect and guide treatment of MDR-TB cases.
- Compliance with recommended biosafety practices and facility design[10]

- Timeliness and effectiveness of information flow from private and public health laboratories to clinicians and TB controllers.
- The capacity to electronically share information and data among laboratorians, clinicians and TB controllers.
- Current legislative mandates and/or other requirements for reporting positive test results to health officials.
- Laboratory proficiency in surge or "ebb" situations.
- Availability of suitable workforce.
- Availability of training for clinicians, laboratorians, TB controllers and other health care providers.

Benchmark 2: Cost Analysis

All states/jurisdictions will perform an **assessment of the true costs of providing TB laboratory services.** Since the cost to identify individual cases rises as the number of cases declines, the cost of services will likely vary from one jurisdiction to another. CDC should provide financial assistance and work with APHL to develop a standardized cost assessment tool that will facilitate comparison of data nationally[7].

Assessment should include costs incurred by public and private laboratories to:

- Provide testing services that meet recommended turn-around times.
- Implement new TB test technologies, as appropriate.
- Provide optimal specimen transport and referral systems.
- Provide training for laboratorians and health care providers.
- Optimize use of conventional and electronic communication systems, including computers and Laboratory Information Management Systems (LIMS) within each jurisdiction to facilitate the timely flow of information among laboratorians, clinicians and TB controllers.

Benchmark 3: Strategic Planning

Jurisdictions will develop a **strategic plan for implementing and maintaining a systems approach to TB control.** CDC should provide the necessary resources and work with appropriate partners to develop recommended testing algorithms for different patient populations, as well as guidelines to help jurisdictions select the appropriate level of service.

The strategic plan should use a systems approach and involve all partners to assure the development, implementation, and ongoing assessment and improvement of a laboratory network that provides:

- Communication and collaboration among all essential partners in TB control.
- Timely, effective reporting and tracking of test results and other information throughout the system. All reporting systems must be NEDSS-compatible and provide for information exchange between the public and private sectors. National standards for reporting fields (results of cultures, molecular detection tests, etc.) would facilitate improved electronic reporting and information flow.
- Mechanisms for efficient specimen and isolate referral for testing performed in both the public and private sectors.
- Use of optimally effective testing algorithms tailored to the needs of the jurisdiction.
- Laboratory staff with a high degree of technical proficiency so that they are able to perform rapid, high quality testing with reliable results.
- Appropriate use of new technologies.
- Timely detection and treatment of MDR-TB cases.
- Rapid TAT for smear and/or NAAT to facilitate moving patients in or out of isolation.
- Facilities and laboratory practices that comply with Biosafety in Microbiological and Biomedical Laboratories[10] (or other current) biosafety recommendations.
- A repository of TB isolates and access to genotyping capability.
- Integrated training activities involving laboratorians, clinicians and TB controllers. (For example, TB controllers and clinicians should be included in technical laboratory training so that they better understand laboratory processes and the impact of laboratory diagnostics on patient management and TB control.)
- Compliance with state/jurisdictional reporting requirements by all network laboratories, including out-of-state commercial laboratories.
- A contingency plan for surge capacity in the event of a TB outbreak or other infectious disease/bioterrorism emergency that could have an impact on TB laboratory services.

Outcome Measures

Once recommended benchmarks have been achieved, the following outcome measures should be used to assess improvements in laboratory services and TB control programs.

- ***TB Incidence Rate***

  Healthy People 2010 objective #14-11 calls for an incidence rate of less than one case per 100,000 people[13]. (Nationally, 6.8 new TB cases per 100,000 population were reported to the National TB Surveillance System in 1998.)

- ***Treatment Initiation***

  All newly diagnosed patients with infectious TB should be started on appropriate treatment within 48 hours of specimen collection.

- ***Average Turn-Around Time***

  Healthy People 2010 objective #14-14 sets a two-day target from receipt of specimen for a laboratory to confirm and report at least 75 percent of TB cases[13]. (Nationally, in 1996 21 days were needed for a laboratory to confirm and report 75 percent of TB cases, according to the CDC's aggregate reports for TB evaluation.)

- ***AFB Smear, Culture and Drug Susceptibility Testing***

  More than 90 percent of laboratories performing TB testing should meet the current CDC recommendations.

- ***Written Procedures for Interaction With TB Control Partners***

  The laboratory should have a *document of understanding* that defines *written procedures* for service provision and communication between the laboratory and TB control partners, including public health agencies, healthcare providers, state TB controllers, etc. The document should include detailed procedures for:

  1. Specimen Submissions—sample collection and transport guidelines, submission forms, recommendations for generating reminders for serial specimen submission, etc.

  2. Determining Appropriateness of Testing Requests—Is the appropriate test being requested? What are the optimum and maximum number of samples that should be submitted for a given patient/site over a specified time period? Etc.

3. Results Notification—smear and culture results, as well as how/where drug susceptibility testing is being ordered, performed, and reported
4. Billing Procedures
5. Process Evaluation

- *Measurement of Training Outcomes*

  Mechanisms to assess training needs and evaluate the effectiveness of training activities are needed. Questions to consider include:

  1. What additional training needs have been identified as a result of a training event?
  2. What modifications in operations have occurred as a result of training?
  3. Have more than 95 percent of specimens received in the laboratory been collected and transported in accord with jurisdictional guidelines?
  4. Do more than 95 percent of the specimens received in the laboratory contain the correct provider and demographic information?

MODELS FOR NETWORK COLLABORATION

There are several successful models for network collaboration for bioterrorism response and the control of TB and other naturally-occurring infectious diseases. A few examples follow.

California MGIT-By-Mail

When CDC cooperative agreement funding for TB control began in the early 1990s, it became apparent that ten small public health laboratories in rural California had insufficient specimen testing volumes to make the use of a selective broth culture system cost-efficient, even though the laboratories had well-trained personnel. Together, the state and local public health laboratories devised an innovative system—originally called *BACTEC-by-Mail*, but later modified to become *MGIT-By-Mail*—to overcome this problem. The new system offers rapid availability of smear results at the local level, as well as access to state-of-the-art rapid methods for culture, identification and susceptibility testing that cannot be made available locally.

Local laboratories receive MGITs (mycobacterial growth indicator tubes) from the state public health laboratory and process specimens for mycobacterial smear and culture on-site, thereby gaining the benefits of rapid TAT for smear results. Processed specimens are inoculated to solid and MGIT culture media. Solid media are incubated and examined locally, but the MGIT tubes are mailed to the state public health laboratory for incubation. State laboratorians then perform positive culture identification using rapid methods, such as DNA probes and high performance liquid chromatography (HPLC), and perform drug susceptibility testing using the radiometric BACTEC method.

Florida Fast Track Referral Model

The Florida Fast Track referral model consolidates advanced TB testing services in the state's two state public health laboratories: a main facility in Jacksonville and a second facility on the campus of AG Holley State Tuberculosis Hospital in Lantana. This system provides participating laboratories with ready access to costly new technologies regardless of local TB test volume. In addition, the TB control program

benefits from having more than 90 percent of all isolates originating within the state submitted into the Florida public health laboratory system, thereby assuring rapid and accurate results with timely reporting.

Both the Jacksonville and the Lantana laboratories perform AFB (acid fast bacillus) smear and sputum processing six days per week. Culture identification, NAAT, and all susceptibility testing (performed using the radiometric BACTEC 460TB system for the four first-line drugs and pyrazinamide) are centralized at the Jacksonville facility and performed seven days per week. The Jacksonville laboratory identifies positive cultures by rapid methods—predominantly using DNA probes or PCR restriction analysis and HPLC—and performs spoligotyping on all isolates of *Mycobacterium tuberculosis*.

Currently specimens are submitted primarily by county health departments, responsible for the care of many of the state's tuberculosis patients, and all smear positive, newly diagnosed patients are automatically *fast-tracked* for NAAT. Hospital laboratories and independent commercial laboratories can refer specimens (including raw sputum) to their local public health laboratory. Samples requiring further tests (AFB smear positive sputum and smear negative samples when clinically indicated) are sent to the state laboratory system with same-day turnaround time for NAAT results. Cultures can also be submitted for final identification and susceptibility testing of TB isolates, as well as the identification of clinically relevant isolates of non-tuberculous mycobacteria. Positive reports are faxed, mailed, and/or electronically downloaded to providers, county health departments, and the state TB control program.

Michigan NLS Model

The National Laboratory System (NLS) model, originally created for biological and chemical terrorism preparedness, is based on an integrated public-private laboratory system that uses standard methods and engages in joint planning and training activities. As one of four NLS pilot sites, Michigan has had an opportunity to apply this model to a broad range of public health concerns, including TB control.

As part of the NLS process, the state laboratory convened partners (clinical microbiology laboratory staff, regional public health laboratory directors, county health department surveillance staff, infection control experts, physicians, physician assistants, and proficiency testing providers) in focus groups to identify the steps necessary to build a jurisdiction-wide laboratory system to support response activities in the event of a public health emergency. Two critical concerns were an improved

specimen transportation system and better communications among partners. (Currently, Michigan's clinical laboratories have varied testing capabilities, but the Michigan Department of Community Health's TB facility is the only laboratory in the state providing comprehensive TB testing services, including HPLC for rapid identification and molecular typing. Thus, transporting specimens to the state laboratory is an important issue for TB control.)

In response to this information, the Michigan public health laboratory is piloting a statewide courier system for overnight delivery of specimens and AFB positive broth cultures to the state TB facility for rapid testing. The goal is to provide 24-hour TAT for AFB slide examinations and rapid culture testing for laboratories that cannot afford to perform their own testing and to provide rapid AFB identification and susceptibility testing to laboratories that already perform rapid culture but do not perform genetic probe or HPLC testing for rapid identifications. In addition, the state public health laboratory is:

- Developing a statewide, Internet-based communication system, the Michigan Disease Surveillance System, to provide epidemiological and laboratory information to health care providers engaged in TB-related work.
- Providing training in the standardized epidemiological and laboratory methods recommended by *Healthy People 2010*, APHL, CDC, and ACET.
- Partnering with commercial laboratories and private health care providers to expedite submission of first isolates from new TB patients for rapid susceptibility testing and molecular typing.

New York State Fast Track Referral Model

The Fast Track model program for tuberculosis was initiated by the New York State Department of Health's Wadsworth Laboratory in 1993 to expedite testing for highly infectious TB patients. Today more than 165 institutions are enrolled in the program. These laboratories process specimens for mycobacterial smear and culture at the local level to provide rapid smear results. Specimens from patients whose smear is positive for AFB, from patients who have a negative smear but radiologic and clinical TB symptoms, and from patients suspected of infection with MDR-TB are fast-tracked to the state public health laboratory for rapid NAAT, liquid and solid media culture, and drug susceptibility testing.

The Fast Track system provides equal access statewide to the latest rapid technology for detection and identification of TB, even for facilities that routinely see little or no TB. Additionally, this system helps to assure that TB cases are

rapidly reported to health department TB control programs (by state laboratorians) and that isolates are captured into the public health system for fingerprinting analysis and outbreak investigations.

North Dakota Consolidation Model

The incidence of TB in North Dakota has declined to a level of less than one percent of state residents each year. Since 1993, the number of specimens coming to the state public health laboratory for testing began to decline steadily until, by 2000, the state laboratory received only about 29 specimens per week—a number low enough to generate concerns about staff proficiency. (The CDC recommends performing more than 20 TB smears per week to maintain proficiency to produce reliable test results.)

State laboratorians wanted to continue their support for the state TB Elimination Program by providing state-of-the-art testing services within recommended TATs, while maintaining the laboratory staff's testing proficiency. In order to do so, they needed to boost test volume. Thus, in 2001 the state public health laboratory developed a strategic plan for TB laboratory services. The laboratory planned to identify medical centers using out-of-state commercial laboratories for TB testing, to determine what services the state laboratory needed to provide to compete with private laboratories, and to improve existing relationships with private clinical laboratories in the state.

Eventually, state laboratorians implemented amplified direct testing with results available within 24 hours of specimen receipt, modified their processing and testing schedules to improve TAT, and met with staff in all of North Dakota's medical centers to improve communication. By educating partners in the state about the needs of the TB control program and the services that the state laboratory could provide, and by delivering reliable test results with quick TATs, the state laboratory has been able to centralize all North Dakota TB testing and to increase its specimen volume to over 45 specimens per week. Moreover, by consolidating testing at the state level, test results are readily available to TB elimination staff.

Washington State Core Laboratory Model

The Washington State Core Laboratory model grew out of a deliberate, carefully planned effort to ensure coordinated delivery of laboratory services within the state in the midst of health care system reforms. The model demonstrates effective public-private partnership to assure that all laboratories have access to state-of-the-art TB testing by consolidating TB diagnostic testing in three *core*, specialty

laboratories—the state public health laboratory and two urban hospital laboratories. All three have on-site access to current technology and adhere to recommended safety and reporting requirements.

Hospital and clinical laboratories are encouraged to submit clinical TB specimens to one of the two core hospital laboratories. The state public health laboratory examines all clinical specimens submitted by local county health departments, serves as the state TB reference laboratory, and maintains capacity to conduct molecular epidemiology studies of TB isolates. It also works with hospital and clinical laboratories that choose to provide limited, on-site TB diagnostic services to ensure that these laboratories meet national TB standards and are integrated into the new delivery system. This model has reduced the clinical workload at the state public health laboratory and simultaneously reduced TATs for reporting smear, culture, and drug susceptibility test results.

Before initiating this system, state laboratorians methodically evaluated the TB diagnostic capacity and expertise in the state and also examined alternative laboratory delivery systems for providing these services. The state public health laboratory:

- Assembled a workgroup to evaluate possible causes of delays in reporting positive test results
- Surveyed laboratories that provided TB testing to document the level of service provided and technology being used
- Conducted on-site reviews of potential core specialty laboratories
- Hosted regional meetings throughout the state to gather input and buy-in from the laboratory community on the new approaches being considered

The Core Laboratory Model debuted in 1999. An evaluation is now underway.

Wisconsin Systems And Laboratory Network Model

The Wisconsin Mycobacteriology Laboratory Network (WMLN), sponsored by the Wisconsin State Laboratory of Hygiene (WSLH) and the state TB control program, is an effective conduit between clinical laboratories and the public health system. The WMLN provides data sharing so that all TB control partners receive regular reports on case counts, outbreaks, and resistance trends. Some services—NAAT, HPLC, and TB identification and molecular subtyping—are centralized at the WSLH. State public health laboratory staff provide technical training to clinical laboratories, as well as a repository for all TB isolates. The TB network also plays a role in bioterrorism (BT) preparedness, since clinical laboratories are prepared to

take on the TB testing currently provided by state laboratorians and to provide personnel trained in BSL-3 practices for BT specimen processing in the event of a BT emergency.

The process of developing the network began with a survey of laboratorians, clinicians and public health professionals to evaluate the role of all state laboratories in TB prevention and control. In 1998 a white paper was developed to describe current practices and lay out recommendations to achieve consistent, high quality testing in all laboratories that performed TB testing. The recommendations addressed appropriate use of NAAT, laboratory safety, staff proficiency, problems with cross-contamination, quality assurance, and more. Beginning in 1999, network members promoted compliance with these recommendations through a series of site visits by WSLH staff and annual meetings with laboratory representatives from across the state.

DISSEMINATION AND IMPLEMENTATION

These recommendations have been approved by the APHL Board of Directors and have been reported to ACET for its consideration and assistance in implementation. To assure their widespread dissemination and implementation, however, key TB control partners must take additional steps:

- APHL, CDC and members of the Task Force will seek opportunities to gain and to **strengthen the support of professional organizations**, including College of American Pathologists (CAP), American Society for Clinical Pathology, ASM, American Clinical Laboratory Association, NTCA, to assure further implementation throughout the healthcare system.
- ACET and its partner organizations must **educate policy makers**, including federal and state legislators and National Governors' Association officers, **to assure that adequate funding is allocated** to implement the recommendations.
- In collaboration with the National Laboratory Training Network, ASM, CAP and NTCA, APHL and CDC will seek opportunities to **develop and deliver integrated training courses** to address laboratory, clinical and TB control issues.
- **APHL and NTCA must build a stronger partnership** and must take advantage of opportunities to exchange information among their members at national meetings, local training forums, etc.

- Expert clinicians, laboratorians, and public health authorities, including representatives of the NTCA, APHL, and the ATS, must work together to **develop templates that are appropriate for high and low incidence regions** and include:

    1. Recommendations for levels of service
    2. Standardized laboratory education materials for clinicians, laboratory staff, public health personnel, and patients
    3. Standardized laboratory requisitions (that might also be used to educate partners).
    4. Notification algorithms
    5. Cost analysis protocol.
    6. Process development (e.g., for analysis and improvement in TAT)
    7. Quality oversight for optimum system performance

RESEARCH NEEDS

Ongoing research needs include:

- Operational research to support science- and experience-based recommendations for laboratory services that provide for effective patient management and population-based TB control.
- Economic research for various types of service and technologies.
- Collaborative technical research to develop and drive the implementation of innovative technologies.

SUMMARY

To eradicate tuberculosis in the United States, clinicians, tuberculosis controllers, and public health officials must have access to timely and reliable TB laboratory services. Delayed laboratory confirmation of tuberculosis leads to delays in initiation of therapy, potentially inappropriate therapy, and missed opportunities to prevent transmission.

Although the provision of laboratory services is a jurisdictional matter, any successful effort to provide timely, reliable laboratory services must involve:

- Assessment and understanding of the structure, performance, and cost of the current network of laboratory service providers and users.
- Development of a referral and information network to ensure reliable testing and timely flow of specimens and information.
- Use of quality improvement principles to continually evaluate and improve the performance of the laboratory service network.

A systems approach is necessary to optimize laboratory TB testing and information exchange and to assure that appropriate services are available in every jurisdiction

A systems approach is necessary to optimize laboratory TB testing and information exchange and to assure that appropriate services are available in every jurisdiction. This report provides guidance on specific action items and performance measures to guide the development and implementation of an integrated system for the provision of laboratory services. Laboratorians, clinicians, public health officials, administrators, and funders must work together to ensure that health care providers and tuberculosis controllers have the information they need to treat tuberculosis patients, block TB transmission and ultimately eliminate the disease in the United States.

REFERENCES

1. Association of Public Health Laboratories. (2002). *Advancing the National Electronic Disease Surveillance System: an essential role for public health laboratories*. Washington, D.C.: Association of Public Health Laboratories.

2. Association of Public Health Laboratories. (2003). *Requirements for public health laboratory information management systems*. Washington, D.C.: Association of Public Health Laboratories.

3. Centers for Disease Control and Prevention. (1992, June 19). National action plan to combat multidrug-resistant tuberculosis. *Morbidity and Mortality Weekly Report*, 41(R-11), 1-48.

4. Centers for Disease Control and Prevention. (1995, August 11). Laboratory practices for diagnosis of tuberculosis—United States, 1994. *Morbidity and Mortality Weekly Report*, 44(31), 587-589.

5. Centers for Disease Control and Prevention. (1999, August 27). Progress toward the elimination of tuberculosis —United States, 1998. *Morbidity and Mortality Weekly Report*, 48(33), 732-736.

6. Geiter, Lawrence. (2000). *Ending neglect, the elimination of tuberculosis in the United States*. Washington, D.C.: National Academy Press.

7. Haddix, A.C.; Teutsch, S.M.; & Corso, P.S. (2000). *Prevention effectiveness: a guide to decision analysis and economic evaluation* (2nd ed.). New York, N.Y.: Oxford University Press, Inc.

8. Kellam, S.; Pascopella, L.; Desmond, E.; Reingold, A.; & Chin, D.P. (2001). Use of recommended laboratory testing methods among patients with tuberculosis in California. *Journal of Clinical Microbiology,* 39, 1969-1971.

9. *Mycobacterium tuberculosis: assessing your laboratory.* (1995). Washington, D.C.: Association of Public Health Laboratories and Centers for Disease Control and Prevention.

10. Richmond, J.Y.; & McKinney, R.W. (1999). *Biosafety in microbiological and biomedical laboratories* (4th ed.). Washington, D.C.: U.S. Government Printing Office.

11. Tenover, F.C.; Crawford, J.T.; Huebner, R.E.; Geiter, L.J.; Horsburgh, C.R. Jr.; & Good, R.C. (1993). The resurgence of tuberculosis: is your laboratory ready? *Journal of Clinical Microbiology*, 31, 767-70.

12. Tokars, J.L.; Rudnick, J.R.; Kroc, K.; Manangan, L.; Puguliese, G; Huebner, R.E.; Chan, J.; & Jarvis, W.R. (1996). U.S. hospital mycobacteriology laboratories: status and comparison with state public health department laboratories. *Journal of Clinical Microbiology*, 34, 680-85.

13. U.S. Department of Health & Human Services. (2000). *Healthy People 2010* (2nd ed.). Washington, D.C.: U.S. Government Printing Office.